REMARKS

Applicants have retained new counsel. Consequently, please **disregard** the Preliminary Amendment filed in connection with the above-captioned patent application on January 23, 2002.

The title has been amended as shown in Appendix A to more accurately reflect the subject matter now claimed. The specification has been amended as shown in Appendix A to correct an error in the naming of the claimed compound, which is discussed in detail below. The sequence listing has been replaced with the listing attached hereto as Appendix B. The attached sequence listing, which is identical to that submitted with the Preliminary Amendment filed January 23, 2002, has been resubmitted to avoid any confusion. In accordance with the requirements of 37 C.F.R. § 1.821(f), it is certified that the contents of the attached paper sequence listing and that of the computer readable copy submitted with this application are the same.

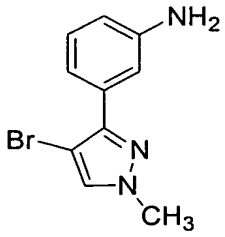
New claims 14-16 are pending in this application. Claims 14 and 15 are supported by the specification as filed. (*See* Experiment 15, page 73, lines 16-26). As discussed below, claim 16 is also supported by the application as filed.

It is well established that a claim may recite an inherent property of an invention described in an application, even if that application does not explicitly disclose the inherent property. *See Kennecott Corp. v. Kyocera International, Inc.*, 835 F.2d 1419, 1423 (Fed. Cir. 1987) ("The disclosure in a subsequent patent application of an inherent property of a product does not deprive that product of the benefit of an earlier filing date. Nor does the inclusion of a description of that property in later-filed claims change this reasonable result"). For example, the Court of Customs and Patent Appeals held on several occasions that the addition to an application of the chemical structure of a compound for which chemical properties had already been disclosed is not new matter. *See, e.g., In re Edwards*, 568 F.2d 1349 (CCPA 1978) (holding that a description of how to make a compound provided support for later filed claims that recited the compound itself); *In re Nathan*, 328 F.2d 1005, 1008 (CCPA 1964) (reversing a rejection of claims that recited the chemical orientation of a compound that was not explicitly described in the patent application, but which was an intrinsic property of the compound for which melting point, optical rotation, ultraviolet spectral analysis and chemical analysis data were provided).

This application describes the synthesis of compounds that modulate serotonin receptors, and which may be useful in the treatment and prevention of a variety of diseases. (Page 3, lines 25-27). Spectroscopic and chromatographic properties of one of those

compounds are described in Experiment 15, which provides the basis for new claims 14 and 15. (Page 73, lines 16-26). In particular, claim 14 recites a serotonin receptor modulator having the ^{1}H NMR spectrum described in Experiment 15, and claim 15 recites a serotonin receptor modulator having the mass spectrum described in Experiment 15. New claim 16 recites a serotonin receptor modulator having the chemical structure of the compound described in Experiment 15. As discussed below, the correct chemical structure of that compound was recently discovered.

The compound described in Experiment 15 was made from a commercially available starting material obtained from Maybridge Chemical Company ("Maybridge"). (Page 55, lines 6-19). After the parent of this application (*i.e.*, application no. 09/292,072) was filed, Applicants discovered that the structure assigned the starting material by Maybridge was incorrect. In particular, it was discovered that the methyl group was attached to the other nitrogen atom of the pyrazole ring, as shown below:



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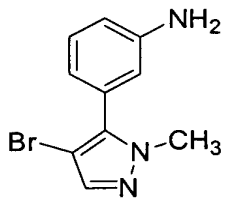
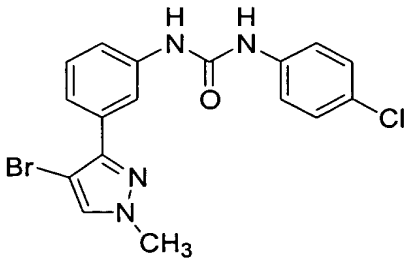


Correct

Unfortunately, the incorrect structure was used to assign a structure to the compound of Experiment 15, which Applicants now realize was incorrect:



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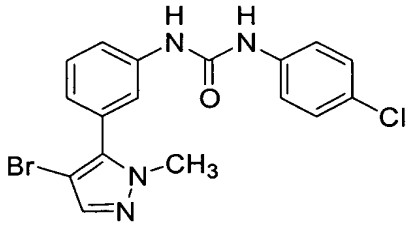

Correct

This realization is based, in part, on Applicants' preparation and testing of a compound that actually does have the structure shown above on the left. As expected, that compound does not possess the same spectroscopic, chemical or biological properties as the compound of the invention, *i.e.*, the compound described in Experiment 15.

It is a fundamental axiom of chemistry that the chemical structure of a compound is an intrinsic property of that compound. Indeed, a compound is defined by its chemical structure. Furthermore, the chemical structure of a compound dictates its physical, chemical and biological properties. For example, the chemical structure of a compound determines its ^{1}H NMR and mass spectra, its chromatographic behavior, and *in vitro* binding affinities. *See, e.g.*, J. McMurry, Organic Chemistry, 411-413 (2nd ed., 1988).

Physical, chemical and biological properties of the compound described in Experiment 15 were measured by Applicants using standard techniques and equipment available to those of ordinary skill in the art, and were described in the application as filed. (*See, e.g.*, page 66, lines 5-21). Those properties include the ^{1}H NMR and mass spectra of the compound (page 73, lines 22-25), its chromatographic behavior under well defined conditions (page 73, lines 20-21, 26; page 66, lines 13-16), and its biological activity as measured using various well defined *in vitro* assays (page 39, second entry in table; page 21, line 15 - page 24, line 7). Like its chemical structure, those properties are inherent properties of the compound described in Experiment 15.

The specification has been amended to correctly name the compound disclosed in Example 15, and new claim 16 recites the correct structure of the compound. Because the structure of the compound is an inherent property of it, and the name of the compound simply reflects that structure using standard nomenclature, Applicants respectfully submit that no new matter has been added by this preliminary amendment. *See, e.g.*, *Kennecott Corp.*, 835 F.2d 1419; *In re Edwards*, 568 F.2d 1349; *In re Nathan*, 328 F.2d 1005.

[remainder of page intentionally left blank]

No fee is believed due for this submission. If one or more fees are due for this submission or to prevent the abandonment of the application, please charge such fee(s) to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date September 24, 2002

45,479

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(212) 790-9090

Attachments

APPENDIX A

Appendix A

Marked-up Version of Amendments to Application No. 10/055,555

In the Title:

Please amend the title as follows:

[NON-ENDOGENOUS, CONSTITUTIVELY ACTIVATED HUMAN] 2-METHYLPYRAZOLE BASED SEROTONIN [RECEPTORS AND SMALL MOLECULE] MODULATORS [THEREOF]

In the Specification:

Please amend the paragraph immediately following the title as follows:

[The benefit of U.S. Serial Number] This application is a continuation of application no. 09/292,072, filed April 14, 1999, which is a continuation-in-part of application no. 09/060,188, filed April 14, 1998 [(owned by Arena Pharmaceuticals, Inc.) and U.S. Provisional Number 60/090,783, filed June 26, 1998 (owned by Arena Pharmaceuticals), U.S. Provisional Number 60/112,909, filed December 18, 1998], and which claims priority to provisional application no. 60/123,000, filed March 5, 1999, provisional application no. 60/112,909, filed December 18, 1998, and provisional application no. [U.S. Provisional Number] 60/090,783, filed June 26, 1998.

Please amend the second chemical name provided in the table on page 39 (*i.e.*, the name provided in the third row of the table below its header) as follows: N-[3-(4-bromo-**[1]**2-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]-carboxamine

Please amend the chemical name provided on page 73, line 18, as follows: N-[3-(4-bromo-**[1]**2-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]-carboxamine

APPENDIX B

SEQUENCE LISTING

<110> Behan, Dominic
Foster, Richard J.
Glen, Robert C.
Lawless, Michael S.
Liu, Qian
Smith, Julian R.
Liaw, Chen W.
Russo, Joseph F.
Thomsen, William J.
Chalmers, Derick

<120> Non-Endogenous, Constitutively Activated Human Serotonin Receptors and Small Molecule Modulators Thereof

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ttcgtgaaca acacgacgtg cgtgctcaac gacccaaatt tcgttcttat tgggtccttc 660

gtagctttct tcataccgct gacgattatg gtgattacgt attgcctgac catctacgtt 720

ctgcgccgac aagctttgat gttactgcac ggccacaccg aggaaccgcc tggactaagt 780

ctggatttcc tgaagtgctg caagaggaat acggccgagg aagagaactc tgcaaaccct 840

aaccaagacc agaacgcacg ccgaagaaag aagaaggaga gacgtcctag gggcaccatg 900

caggctatca acaatgaaag aaaagctaag aaagtccttg ggattgtttt ctttgtgttt 960

ctgatcatgt ggtgcccatt tttcattacc aatattctgt ctgttctttg tgagaagtcc 1020

tgtaaccaaa agctcatgga aaagcttctg aatgtgtttg tttggattgg ctatgtttgt 1080

tcaggaatca atcctctggt gtatactctg ttcaacaaaa tttaccgaag ggcattctcc 1140

aactatttgc gttgcaatta taaggtagag aaaaagcctc ctgtcaggca gattccaaga 1200

gttgccgcca ctgctttgtc tgggagggag cttaatgtta acatttatcg gcataccaat 1260

gaaccggtga tcgagaaagc cagtgacaat gagcccggta tagagatgca agttgagaat 1320

ttagagttac cagtaaatcc ctccagtgtg gttagcgaaa ggattagcag tgtgtga 1377

<210> 29
<211> 458
<212> PRT
<213> Artificial Sequence

<220>
<223> Novel Sequence

<400> 29

Met Val Asn Leu Arg Asn Ala Val His Ser Phe Leu Val His Leu Ile
1 5 10 15

Gly Leu Leu Val Trp Gln Cys Asp Ile Ser Val Ser Pro Val Ala Ala
20 25 30

Ile Val Thr Asp Ile Phe Asn Thr Ser Asp Gly Gly Arg Phe Lys Phe
35 40 45

Pro Asp Gly Val Gln Asn Trp Pro Ala Leu Ser Ile Val Ile Ile Ile
50 55 60

Ile Met Thr Ile Gly Gly Asn Ile Leu Val Ile Met Ala Val Ser Met
65 70 75 80

Glu Lys Lys Leu His Asn Ala Thr Asn Tyr Phe Leu Met Ser Leu Ala
85 90 95

Ile Ala Asp Met Leu Val Gly Leu Leu Val Met Pro Leu Ser Leu Leu
100 105 110

Ala Ile Leu Tyr Asp Tyr Val Trp Pro Leu Pro Arg Tyr Leu Cys Pro
115 120 125

Val Trp Ile Ser Leu Asp Val Leu Phe Ser Thr Ala Ser Ile Met His
130 135 140

Leu Cys Ala Ile Ser Leu Asp Arg Tyr Val Ala Ile Arg Asn Pro Ile
145 150 155 160

Glu His Ser Arg Phe Asn Ser Arg Thr Lys Ala Ile Met Lys Ile Ala
165 170 175

Ile Val Trp Ala Ile Ser Ile Gly Val Ser Val Pro Ile Pro Val Ile
180 185 190

Gly Leu Arg Asp Glu Glu Lys Val Phe Val Asn Asn Thr Thr Cys Val
195 200 205

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Leu Asn Asp Pro Asn Phe Val Leu Ile Gly Ser Phe Val Ala Phe Phe
    210                 215                 220

Ile Pro Leu Thr Ile Met Val Ile Thr Tyr Cys Leu Thr Ile Tyr Val
225                 230                 235                 240

Leu Arg Arg Gln Ala Leu Met Leu Leu His Gly His Thr Glu Glu Pro
                245                 250                 255

Pro Gly Leu Ser Leu Asp Phe Leu Lys Cys Cys Lys Arg Asn Thr Ala
            260                 265                 270

Glu Glu Glu Asn Ser Ala Asn Pro Asn Gln Asp Gln Asn Ala Arg Arg
        275                 280                 285

Arg Lys Lys Lys Glu Arg Arg Pro Arg Gly Thr Met Gln Ala Ile Asn
    290                 295                 300

Asn Glu Arg Lys Ala Lys Lys Val Leu Gly Ile Val Phe Phe Val Phe
305                 310                 315                 320

Leu Ile Met Trp Cys Pro Phe Phe Ile Thr Asn Ile Leu Ser Val Leu
                325                 330                 335

Cys Glu Lys Ser Cys Asn Gln Lys Leu Met Glu Lys Leu Leu Asn Val
            340                 345                 350

Phe Val Trp Ile Gly Tyr Val Cys Ser Gly Ile Asn Pro Leu Val Tyr
        355                 360                 365

Thr Leu Phe Asn Lys Ile Tyr Arg Arg Ala Phe Ser Asn Tyr Leu Arg
    370                 375                 380

Cys Asn Tyr Lys Val Glu Lys Lys Pro Pro Val Arg Gln Ile Pro Arg
385                 390                 395                 400

Val Ala Ala Thr Ala Leu Ser Gly Arg Glu Leu Asn Val Asn Ile Tyr
                405                 410                 415

Arg His Thr Asn Glu Pro Val Ile Glu Lys Ala Ser Asp Asn Glu Pro
            420                 425                 430

Gly Ile Glu Met Gln Val Glu Asn Leu Glu Leu Pro Val Asn Pro Ser
        435                 440                 445

Ser Val Val Ser Glu Arg Ile Ser Ser Val
    450                 455
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<210> 30
<211> 1437
<212> DNA

<213> Artificial Sequence

<220>
<223> Novel Sequence

<400> 30
atggatattc tttgtgaaga aaatacttct ttgagctcaa ctacgaactc cctaatgcaa 60

ttaaatgatg acaacaggct ctacagtaat gactttaact ccggagaagc taacacttct 120

gatgcattta actggacagt cgactctgaa aatcgaacca acctttcctg tgaagggtgc 180

ctctcaccgt cgtgtctctc cttacttcat ctccaggaaa aaaactggtc tgctttactg 240

acagccgtag tgattattct aactattgct ggaaacatac tcgtcatcat ggcagtgtcc 300

ctagagaaaa agctgcagaa tgccaccaac tatttcctga tgtcacttgc catagctgat 360

atgctgctgg gtttccttgt catgcccgtg tccatgttaa ccatcctgta tgggtaccgg 420

tggcctctgc cgagcaagct ttgtgcagtc tggatttacc tggacgtgct cttctccacg 480

gcctccatca tgcacctctg cgccatctcg ctggaccgct acgtcgccat ccagaatccc 540

atccaccaca gccgcttcaa ctccagaact aaggcatttc tgaaaatcat tgctgtttgg 600

accatatcag taggtatatc catgccaata ccagtctttg ggctacagga cgattcgaag 660

gtctttaagg aggggagttg cttactcgcc gatgataact ttgtcctgat cggctctttt 720

gtgtcatttt tcattccctt aaccatcatg gtgatcacct actttctaac tatcaaggtt 780

ctgcgccgac aagctttgat gttactgcac ggccacaccg aggaaccgcc tggactaagt 840

ctggatttcc tgaagtgctg caagaggaat acggccgagg aagagaactc tgcaaaccct 900

aaccaagacc agaacgcacg ccgaagaaag aagaaggaga gacgtcctag gggcaccatg 960

caggctatca acaatgaaag aaaagcttcg aaggtactgg gcatcgtctt cttcctgttt 1020

gtggtgatgt ggtgcccttt cttcatcaca aacatcatgg ccgtcatctg caaagagtcc 1080

tgcaatgagg atgtcattgg ggccctgctc aatgtgtttg tttggatcgg ttatctctct 1140

tcagcagtca acccactagt ctatactctg ttcaacaaaa tttaccgaag ggcattctcc 1200

aactatttgc gttgcaatta taaggtagag aaaaagcctc ctgtcaggca gattccaaga 1260

gttgccgcca ctgctttgtc tgggagggag cttaatgtta acatttatcg gcataccaat 1320

gaaccggtga tcgagaaagc cagtgacaat gagcccggta tagagatgca agttgagaat 1380

ttagagttac cagtaaatcc ctccagtgtg gttagcgaaa ggattagcag tgtgtga 1437

<210> 31
<211> 478
<212> PRT
<213> Artificial Sequence

<220>
<223> Novel Sequence

<400> 31

Met Asp Ile Leu Cys Glu Glu Asn Thr Ser Leu Ser Ser Thr Thr Asn
1 5 10 15

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Ser Leu Met Gln Leu Asn Asp Asp Asn Arg Leu Tyr Ser Asn Asp Phe
            20                  25                  30

Asn Ser Gly Glu Ala Asn Thr Ser Asp Ala Phe Asn Trp Thr Val Asp
        35                  40                  45

Ser Glu Asn Arg Thr Asn Leu Ser Cys Glu Gly Cys Leu Ser Pro Ser
    50                  55                  60

Cys Leu Ser Leu Leu His Leu Gln Glu Lys Asn Trp Ser Ala Leu Leu
65                  70                  75                  80

Thr Ala Val Val Ile Ile Leu Thr Ile Ala Gly Asn Ile Leu Val Ile
                85                  90                  95

Met Ala Val Ser Leu Glu Lys Lys Leu Gln Asn Ala Thr Asn Tyr Phe
            100                 105                 110

Leu Met Ser Leu Ala Ile Ala Asp Met Leu Leu Gly Phe Leu Val Met
        115                 120                 125

Pro Val Ser Met Leu Thr Ile Leu Tyr Gly Tyr Arg Trp Pro Leu Pro
    130                 135                 140

Ser Lys Leu Cys Ala Val Trp Ile Tyr Leu Asp Val Leu Phe Ser Thr
145                 150                 155                 160

Ala Ser Ile Met His Leu Cys Ala Ile Ser Leu Asp Arg Tyr Val Ala
                165                 170                 175

Ile Gln Asn Pro Ile His His Ser Arg Phe Asn Ser Arg Thr Lys Ala
            180                 185                 190

Phe Leu Lys Ile Ile Ala Val Trp Thr Ile Ser Val Gly Ile Ser Met
        195                 200                 205

Pro Ile Pro Val Phe Gly Leu Gln Asp Asp Ser Lys Val Phe Lys Glu
    210                 215                 220

Gly Ser Cys Leu Leu Ala Asp Asp Asn Phe Val Leu Ile Gly Ser Phe
225                 230                 235                 240

Val Ser Phe Phe Ile Pro Leu Thr Ile Met Val Ile Thr Tyr Phe Leu
                245                 250                 255

Thr Ile Lys Val Leu Arg Arg Gln Ala Leu Met Leu Leu His Gly His
            260                 265                 270

Thr Glu Glu Pro Pro Gly Leu Ser Leu Asp Phe Leu Lys Cys Cys Lys
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275 280 285

Arg Asn Thr Ala Glu Glu Glu Asn Ser Ala Asn Pro Asn Gln Asp Gln
290 295 300

Asn Ala Arg Arg Arg Lys Lys Lys Glu Arg Arg Pro Arg Gly Thr Met
305 310 315 320

Gln Ala Ile Asn Asn Glu Arg Lys Ala Ser Lys Val Leu Gly Ile Val
325 330 335

Phe Phe Leu Phe Val Val Met Trp Cys Pro Phe Phe Ile Thr Asn Ile
340 345 350

Met Ala Val Ile Cys Lys Glu Ser Cys Asn Glu Asp Val Ile Gly Ala
355 360 365

Leu Leu Asn Val Phe Val Trp Ile Gly Tyr Leu Ser Ser Ala Val Asn
370 375 380

Pro Leu Val Tyr Thr Leu Phe Asn Lys Ile Tyr Arg Arg Ala Phe Ser
385 390 395 400

Asn Tyr Leu Arg Cys Asn Tyr Lys Val Glu Lys Lys Pro Pro Val Arg
405 410 415

Gln Ile Pro Arg Val Ala Ala Thr Ala Leu Ser Gly Arg Glu Leu Asn
420 425 430

Val Asn Ile Tyr Arg His Thr Asn Glu Pro Val Ile Glu Lys Ala Ser
435 440 445

Asp Asn Glu Pro Gly Ile Glu Met Gln Val Glu Asn Leu Glu Leu Pro
450 455 460

Val Asn Pro Ser Ser Val Val Ser Glu Arg Ile Ser Ser Val
465 470 475

<210> 32
<211> 1437
<212> DNA
<213> Artificial Sequence

<220>
<223> Novel Sequence

<400> 32
atggatattc tttgtgaaga aaatacttct ttgagctcaa ctacgaactc cctaatgcaa 60

ttaaatgatg acaacaggct ctacagtaat gactttaact ccggagaagc taacacttct 120

gatgcattta actggacagt cgactctgaa aatcgaacca acctttcctg tgaagggtgc 180

ctctcaccgt cgtgtctctc cttacttcat ctccaggaaa aaaactggtc tgctttactg 240

acagccgtag tgattattct aactattgct ggaaacatac tcgtcatcat ggcagtgtcc 300

ctagagaaaa agctgcagaa tgccaccaac tatttcctga tgtcacttgc catagctgat 360

atgctgctgg gtttccttgt catgcccgtg tccatgttaa ccatcctgta tgggtacegg 420

tggcctctgc cgagcaagct ttgtgcagtc tggatttacc tggacgtgct cttctccacg 480

gcctccatca tgcacctctg cgccatctcg ctggaccgct acgtcgccat ccagaatccc 540

atccaccaca gccgcttcaa ctccagaact aaggcatttc tggaaaatcat tgctgtttgg 600

accatatcag taggtatatc catgccaata ccagtctttg ggctacagga cgattcgaag 660

gtctttaagg aggggagttg cttactcgcc gatgataact ttgtcctgat cggctctttt 720

gtgtcatttt tcattcccct gacgattatg gtgattacgt attgcctgac catctacgtt 780

ctgcgccgac aagctttgat gttactgcac ggccacaccg aggaaccgcc tggactaagt 840

ctggatttcc tgaagtgctg caagaggaat acggccgagg aagagaactc tgcaaaccct 900

aaccaagacc agaacgcacg ccgaagaaag aagaaggaga gacgtcctag gggcaccatg 960

caggctatca acaatgaaag aaaagctaag aaagtccttg ggattgtttt ctttgtgttt 1020

ctgatcatgt ggtgcccttt cttcatcaca aacatcatgg ccgtcatctg caaagagtcc 1080

tgcaatgagg atgtcattgg ggccctgctc aatgtgtttg tttggatcgg ttatctctct 1140

tcagcagtca acccactagt ctatactctg ttcaacaaaa tttaccgaag ggcattctcc 1200

aactatttgc gttgcaatta taaggtagag aaaaagcctc ctgtcaggca gattccaaga 1260

gttgccgcca ctgctttgtc tgggagggag cttaatgtta acatttatcg gcataccaat 1320

gaaccggtga tcgagaaagc cagtgacaat gagcccggta tagagatgca agttgagaat 1380

ttagagttac cagtaaatcc ctccagtgtg gttagcgaaa ggattagcag tgtgtga 1437

<210> 33
<211> 478
<212> PRT
<213> Artificial Sequence

<220>
<223> Novel Sequence

<400> 33

Met Asp Ile Leu Cys Glu Glu Asn Thr Ser Leu Ser Ser Thr Thr Asn
1 5 10 15

Ser Leu Met Gln Leu Asn Asp Asp Asn Arg Leu Tyr Ser Asn Asp Phe
20 25 30

Asn Ser Gly Glu Ala Asn Thr Ser Asp Ala Phe Asn Trp Thr Val Asp
35 40 45

Ser Glu Asn Arg Thr Asn Leu Ser Cys Glu Gly Cys Leu Ser Pro Ser
50 55 60

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Cys Leu Ser Leu Leu His Leu Gln Glu Lys Asn Trp Ser Ala Leu Leu
65                  70                  75                  80

Thr Ala Val Val Ile Ile Leu Thr Ile Ala Gly Asn Ile Leu Val Ile
                85                  90                  95

Met Ala Val Ser Leu Glu Lys Lys Leu Gln Asn Ala Thr Asn Tyr Phe
            100                 105                 110

Leu Met Ser Leu Ala Ile Ala Asp Met Leu Leu Gly Phe Leu Val Met
        115                 120                 125

Pro Val Ser Met Leu Thr Ile Leu Tyr Gly Tyr Arg Trp Pro Leu Pro
    130                 135                 140

Ser Lys Leu Cys Ala Val Trp Ile Tyr Leu Asp Val Leu Phe Ser Thr
145                 150                 155                 160

Ala Ser Ile Met His Leu Cys Ala Ile Ser Leu Asp Arg Tyr Val Ala
                165                 170                 175

Ile Gln Asn Pro Ile His His Ser Arg Phe Asn Ser Arg Thr Lys Ala
            180                 185                 190

Phe Leu Lys Ile Ile Ala Val Trp Thr Ile Ser Val Gly Ile Ser Met
        195                 200                 205

Pro Ile Pro Val Phe Gly Leu Gln Asp Asp Ser Lys Val Phe Lys Glu
    210                 215                 220

Gly Ser Cys Leu Leu Ala Asp Asp Asn Phe Val Leu Ile Gly Ser Phe
225                 230                 235                 240

Val Ser Phe Phe Ile Pro Leu Thr Ile Met Val Ile Thr Tyr Cys Leu
                245                 250                 255

Thr Ile Tyr Val Leu Arg Arg Gln Ala Leu Met Leu Leu His Gly His
            260                 265                 270

Thr Glu Glu Pro Pro Gly Leu Ser Leu Asp Phe Leu Lys Cys Cys Lys
        275                 280                 285

Arg Asn Thr Ala Glu Glu Glu Asn Ser Ala Asn Pro Asn Gln Asp Gln
    290                 295                 300

Asn Ala Arg Arg Arg Lys Lys Lys Glu Arg Arg Pro Arg Gly Thr Met
305                 310                 315                 320

Gln Ala Ile Asn Asn Glu Arg Lys Ala Lys Lys Val Leu Gly Ile Val
                325                 330                 335
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Phe Phe Val Phe Leu Ile Met Trp Cys Pro Phe Phe Ile Thr Asn Ile
            340                 345                 350

Met Ala Val Ile Cys Lys Glu Ser Cys Asn Glu Asp Val Ile Gly Ala
        355                 360                 365

Leu Leu Asn Val Phe Val Trp Ile Gly Tyr Leu Ser Ser Ala Val Asn
    370                 375                 380

Pro Leu Val Tyr Thr Leu Phe Asn Lys Ile Tyr Arg Arg Ala Phe Ser
385                 390                 395                 400

Asn Tyr Leu Arg Cys Asn Tyr Lys Val Glu Lys Lys Pro Pro Val Arg
                405                 410                 415

Gln Ile Pro Arg Val Ala Ala Thr Ala Leu Ser Gly Arg Glu Leu Asn
            420                 425                 430

Val Asn Ile Tyr Arg His Thr Asn Glu Pro Val Ile Glu Lys Ala Ser
        435                 440                 445

Asp Asn Glu Pro Gly Ile Glu Met Gln Val Glu Asn Leu Glu Leu Pro
    450                 455                 460

Val Asn Pro Ser Ser Val Val Ser Glu Arg Ile Ser Ser Val
465                 470                 475
```